

THE EFFECT OF ACUTE OVARIECTOMY ON RABBIT BLADDER BLOOD FLOW AND OXYGEN TENSION

Hypothesis / aims of study

Recent studies have demonstrated that urinary bladder structure and function can be significantly affected by alterations in circulating estrogen. In women, reduction of circulating estrogen after menopause has been associated with bladder dysfunction; in rabbits, decreases in circulating estrogen have resulted in mucosal hypoxia, apoptosis, and atrophy. In the present studies, we determined the effect of acute ovariectomy on rabbit bladder blood flow and tissue oxygenation.

Study design, materials and methods

Female New Zealand White rabbits were ovariectomized and evaluated at 1, 3, and 7 days post-ovariectomy. Sham surgeries were used as controls. Tissue blood flow and tissue oxygen tension were measured in vivo with an Oxylab multi-purpose monitor and probe. This instrument simultaneously measures in real time blood flow in arbitrary Blood Perfusion Units (BPU) and PO₂ in mm Hg. Each rabbit was injected 2 hours before the study with 10 mg / kg hypoxypote-1. Tissue hypoxia was demonstrated with hypoxypote-1 immunohistochemistry.

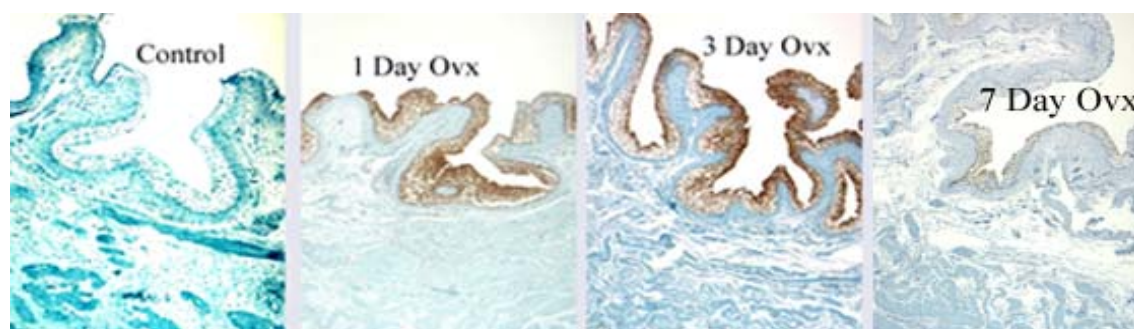
Results

Acute ovariectomy resulted in a significant decrease in urothelial oxygen tension as soon as day 1, and a trend toward decreased urothelial blood flow. Bladder muscle did not demonstrate hypoxia post-ovariectomy, and muscle blood flow trended lower at days 1 and 3, returning to baseline by day 7 (see table).

	Mucosa pO ₂	Muscle pO ₂	Mucosa BPU	Muscle BPU
Control - Sham	16.1 +/- 2.2	11.1 +/- 1.7	1228.0 +/- 156.8	638.6 +/- 105.6
1 Day Ovariectomy	2.7 +/- 1.1 *	11.6 +/- 1.5	1120.8 +/- 127.4	523.6 +/- 103.5
3 Day Ovariectomy	2.6 +/- 0.6 *	12.6 +/- 1.3	970.6 +/- 247.0	420.2 +/- 106.9
7 Day Ovariectomy	5.1 +/- 1.7 *	8.1 +/- 1.4	890.4 +/- 91.7	638.5 +/- 65.7

* = significantly below control, p < 0.05

Hypoxypote immunohistochemistry confirmed the presence of urothelial hypoxia and endothelial hypoxia after ovariectomy at all time periods, although the density was significantly lighter at 7 days. Sham surgery did not have any effect on either blood flow or PO₂. Immunohistochemistry showed no hypoxia within the bladder muscle or mucosa.



Hypoxy Probe Immunohistochemistry

Interpretation of results

This study demonstrates that the urothelium is extremely sensitive to acute ovariectomy, with significant urothelial hypoxia seen by post-ovariectomy day 1. Mucosal blood flow also trended lower post-ovariectomy, while the effects on bladder muscle oxygenation and

perfusion were small. Short duration physiologic reduction in estrogen in menstruating females may cause similar episodes of hypoxia within the urothelium.

Concluding message

Sensory nerves are localized in the submucosa, an area that displays frank hypoxia following ovariectomy. We believe that in women, cyclical changes in estrogen that occur during the menstrual cycle may result in cyclical hypoxia within the mucosa and submucosa, and since sensory nerves are very sensitive to hypoxic damage, this may be one of the etiological factors in pelvic pain syndromes and conditions such as interstitial cystitis.

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